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14. ABSTRACT

We produce unusual DNA motifs from synthetic oligonucleotides. We use these molecules individually or in combinations to produce systems to implement DNA nanotechnology. Computer optimization of DNA sequences is used to select the molecules to synthesize. Structures are assembled in solution, and 1D or 2D arrays are deposited on mica for characterization by AFM. 3D arrays are analyzed by X-ray diffraction. During the current project period, we have built a robust DNA nanomechanical device and a nanorobot that walks on a sidewalk. We have built robust 2D arrays, and have made large strides towards the control of matter in 3D.

15. SUBJECT TERMS

Unusual DNA Motifs; Nanorobotics; 3D Structural Control; DNA Nanotechnology

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FINAL REPORT

GRANT #: N00014-98-1-0093

PRINCIPAL INVESTIGATOR: Dr. Nadrian C. Seeman

INSTITUTION: New York University

GRANT TITLE: Macromolecular Design

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OBJECTIVE: To develop and extend the methods of DNA nanotechnology to gain control over the structure of matter in 2D and in 3D and to produce DNA-based nanorobots.

APPROACH; Branched DNA motifs are designed by use of an algorithm that minimizes sequence symmetry. Oligonucleotides corresponding to these sequences are then assembled. These motifs are then assembled primarily by using cooling protocols. The resulting structures are examined by AFM, by gel electrophoresis or by X-ray diffraction, as appropriate to the target construct.

ACCOMPLISHMENTS:

Advances in Algorithmic Assembly: We have demonstrated successful algorithmic assembly leading to a cumulative XOR calculation (#1). This was a major step in DNA self-assembly, the first time that algorithmic assembly was demonstrated. Having shown the feasibility of aperiodic assembly, we have participated in several studies in the theory of aperiodic self-assembly (#13, #16, #26, #32, #33, #39) and other aspects of DNA-based computation (#41); this work include experimental studies (#20, #23, #29, #35) that entail making irregular graphs from DNA.

2D and 3D Arrays: We have developed (#3) and applied (#22) a quantitative ligation-closure method to demonstrate that the DX motif is about twice as stiff as ordinary DNA. We have used this information to develop robust geometrical motifs, such as the DX-triangle (#44), which forms a honey-comb array. This is a decade-old goal, on which we failed repeatedly before finally achieving this success.

We have been engaged in crystallographic studies during the current project period, partly to establish the nature of the 3D materials that we have built. Our preliminary results (#45) demonstrate the correct unit cell dimensions and space groups for a motif containing tensegrity triangles. As suggested by the results for the pseudo-hexagonal system, we are building DX versions of these triangles and we will use them to try to build crystals. We have also discovered new parallel non-Watson-Crick pairing motifs in the crystal structure of a DNA 13-mer (#42).

We were successful in demonstrating our specific aim of paranemic cohesion (#14), but this approach has not yet been shown to be useful in array construction. We are trying to get it to work in 2D.

We used AFM to demonstrate successfully the structure of 'Bowtie' junctions (#2), demonstrating the robustness of the parallelogram motif in V-shaped and 2D arrays.

Nanomechanical Devices: We have established general principles for the creation of motifs in DNA (#7); it is now straightforward to develop new motifs for different purposes, as demonstrated by our development of the PX motif (#31) and its used in both paranemic cohesion (#14), and, more importantly, in the development of the robust sequence-dependent PX-JX_2 device (#8). The development of PX-JX_2 device required the construction of edge-sharing motifs (#21) for its demonstration by AFM.

A second device that we developed is a prototypical nanorobot that walks on a sidewalk (#36). Using the Yurke method of strand removal, its attachment points to the sidewalk are altered in the course of its taking a step.

A third device measures the amount of work a DNA-distorting protein can perform as a consequence of binding to its target (#43). This device was prototyped with integration host factor (IHF), and is similar to a B-Z device developed in a previous project period. IHF binds to its recognition site, and distorts the DNA there. However, to do so, it must break base pairs, so that the amount of work it can do can be estimated by the load against which it cannot work.

We have also prototyped a translational device based on the PX-JX_2 device. It contains two such devices separating two clamps that can contain a DX motif with a continuous strand. The two different devices lead to four different states, and four different polymers, although in this case the polymers are all DNA. As a consequence of the strands added to set the states of the two devices, a variety of different polymers are made (#46).

Scaffolding Non-DNA Materials: For several project periods, we have suggested that DNA nanotechnology would be a feasible method for scaffolding other materials. During this project period, we have begun to prototype this chemistry through various collaborators. These efforts have led to the organization of gold nanoparticles (with Rick Kiehl of Minnesota) (#15) and the scaffolding of industrial polymers on a nucleic acid backbone (with Jim Canary of NYU) (#17, #25). In addition, we have explored neutralizing components of DNA arrays by incorporating peptide-nucleic acid units (PNA) with the arrays (#37). The essence of these studies is the addition of functionality to nucleic acid arrays.

Dissemination of Progress:

The development of structural DNA nanotechnology has struck the fancy of the scientific community, resulting in many requests for review articles (#4, #5, #6, #9, #10, #11, #12, #18, #19, #24, #27, #28, #30, #34, #38, #40), where # is the serial number in the publications list.

CONCLUSIONS: Structurally based DNA nanotechnology has been shown to be an extremely potent method of controlling the structure of matter on the nanometer scale. Particularly noteworthy advances during this project period include the establishment of the robustness of DX cohesion (#44), the construction of robust sequence-dependent devices (#8 and #46), the use of DNA in algorithmic assembly (#1), the development of paranemic cohesion (#14), the one-pot synthesis of an irregular graph (#35), and the incorporation of non-DNA materials in DNA-based constructs.

SIGNIFICANCE: The results presented here demonstrate that DNA-based nanotechnology is a powerful way of creating designed structures and devices.

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6. S. Liao & N.C. Seeman, A Polynucleotide Nanomechanical Device that Acts as an Artificial Ribosome and Translates DNA Signals into Polymer Assembly Instructions, #60/592,402, Filed, 08/02/04.

AWARD INFORMATION: Appointed to the Margaret and Herman Sokol Chair in Chemistry at NYU; recipient of the Tulip Award as the outstanding scientist of the year by the DNA-Based Computation community.

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